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A comparative evaluation of ischemic mitral regurgitation in AMI patients managed by revascularization Vs optimal medical therapy

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ABSTRACT

Background: Ischemic heart disease is the leading cause of death worldwide. Mitral regurgitation is one of the common complications associated with acute coronary syndromes leading to high morbidity and mortality. **Aims and Objectives:** Ischemic mitral regurgitation (IMR) is one of the frequent complications associated with coronary artery disease (CAD); but the optimal management of IMR is controversial. Our aim was to evaluate and compare the impact of medical therapy versus revascularization on the degree of MR. **Materials and Methods:** We performed observational follow up study on 114 patients admitted to our hospital with AMI and mild to moderate degree of MR. Multiple parameters were used to assess the severity of MR at baseline and after 1 year of follow up to assess the change in MR severity after medial therapy and revascularization. **Results:** In the medically managed group, MR grade improved in 28.57% of patients while 53.57% patients remained in the same grade as before. The grade of MR deteriorated from moderate to severe in 17.86% patients during follow up. In revascularization group; improvement in MR grade was observed in 60.71% of patients while 32.14% patients remained in the previous grade. Deterioration from moderate to severe occurred in 7.14% of patients. PCI and CABG subgroup analysis showed almost similar impact on degree of MR during follow up. **Conclusion:** From our study we concluded that revascularization; either in form of PCI or CABG, is associated with improvement in degree of MR when compared to optimal medical therapy alone.

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INTRODUCTION

Coronary artery disease is one of the leading causes of death worldwide. Ischemic mitral regurgitation (IMR) is defined as mitral regurgitation complicating the manifestations of CAD in the absence of primary leaflet or chordal pathology.[1] Many studies have shown that IMR is an independent predictor of cardiovascular morbidity and mortality. Its presence is associated with a three-fold increase in the risk of heart failure and a 1.6-fold increased risk of death at 5-year follow-up, independent of LV ejection fraction, Killip class, age and gender.[2] The increased mortality risk relates to the quantified degree of MR; as survival rates are different between patients with different degrees of IMR.[3] The pathophysiology of IMR is complex, and its presence may be related to several underlying processes that are often difficult to separate in a given patient.[4] Because of its complex pathophysiology and heterogeneous clinical presentation, the proper treatment of IMR is often debated, and the relative utility of revascularization is uncertain.[5]

Few studies have shown that revascularization is associated with improved survival compared with medical therapy in patients with IMR,[6,7] but the proper way of revascularization still remains controversial. Surgical revascularization has potential benefits of achieving more

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complete revascularization and improving IMR more effectively by addition of a mitral valve procedure at the time of coronary artery bypass graft (CABG) surgery. However, surgical revascularization has a higher procedural risk compared with percutaneous coronary intervention (PCI), and it is unclear whether IMR is merely a marker for more advanced left ventricular (LV) dysfunction or whether IMR itself should be a target for therapy.[8] In previous studies, MV surgery in addition to CABG was not associated with an incremental reduction in mortality beyond PCI and CABG alone.[9,10]

MATERIALS AND METHODS

Patient selection

Patients were divided into two groups based on their line of management. Group- A included patients managed with optimal medical therapy (OMT) while Group- B included patients managed with revascularization. Subgroups B1 & B2 included patients managed with PCI and CABG respectively. Patients having concomitant rheumatic heart disease or documented mitral regurgitation due to any other pathology were excluded from the study. Patients with severe MR or any other mechanical complications associated with acute myocardial infarction were also excluded from the study.

Study parameters for defining MR severity

There are various parameters to define the severity of MR but some disparity persists among the guidelines as to what constitutes severe MR.[11] Almost all the guidelines agree that EROA ≥0.4 cm^2, RgV ≥60 mL, and RgF ≥50% constitute severe MR.[12-15] These numbers are derived from a study that calibrated echo data with biplane angiographic grading.[16] The above values had the optimal sensitivity and specificity for 4+ angiographic MR. The cutoff values for ≥3+ angiographic MR severity were EROA ≥0.3 cm^2, RgV ≥45 mL, and RgF ≥40%. The 2 published randomized trials in MR, Acorn and EVEREST II used ≥3+ as entry criteria.[17-19] The Cardiothoracic Surgery Network trials originally used EROA ≥0.4 cm^2 for the severe MR trial[20] and 0.2 to 0.39 cm^2 for the moderate MR trial[21] which were subsequently modified to allow lower values for EROA if accompanied by other echo signs that indicated that MR severity was worse, such as RgV, VCW etc. Considering above points, following parameters were studied to grade the severity of MR in our study:

Distal MR jet area compared to LA

The high turbulent mosaic color Doppler pattern of MR flow was measured as a ratio relative to the left atrial area. Traced at its maximum in apical views, the MR jet area was divided by the left atrial area traced in same frame.[22] As per the measurements, MR was divided into mild (<20%), moderate (20-39%) and severe (≥40%).

Vena contracta width (VCW)

The VCW was measured as the linear dimension of the neck of the MR jet in parasternal long axis plane.[23] As per measurements, MR was categorised as mild (<0.3 cm), moderate (0.3cm- <0.7cm) and severe (≥0.7cm).[14,15]

Proximal isovelocity surface area (PISA)

PISA was used (where feasible) to calculate the EROA and mitral RgV as follows[24]:

Flow rate at PISA=flow rate across regurgitant orifice

$$2\pi r2 \times \text{Aliasing velocity} = \text{EROA} \times \text{MR velocity}$$

$$\text{EROA} = 2\pi r2 \times \text{Aliasing velocity} \div \text{MR velocity}$$

(r= radius of the hemispheric PISA zone)

$$\text{Mitral RgV} = \text{EROA} \times \text{TVI of MR}$$

Based on the RgV, MR was quantified into mild (<30 ml), moderate (30-59 ml) and severe (≥60 ml).

Volumetric method

Based on the principle that without notable aortic regurgitation, MR volume is the difference between the flow across the mitral valve and the LVOT. The regurgitant fraction (RgF) was calculated by dividing RgV by flow across the mitral valve and multiplied by 100.[25,26]

$$\text{MV flow} = \text{LVOT flow} + \text{MV RgV}$$

$$\text{MV RgV} = \text{MV flow} - \text{LVOT flow}$$

$$\text{MV Rg V} = \text{Mitral annular area MV TVI} - \text{Aortic annulus area LVOT TVI}$$

$$\text{Mitral RgF} = \text{MV Rg V MV flow 100}$$

Based on RgF, MR was divided into mild (<30%), moderate (30-49%) and severe (≥50%).

Statistical analysis

The completed data was analyzed by using standard statistical methods. Statistical tools like mean (μ) and standard deviations (SD) were calculated and information obtained from these statistical derivatives were used to calculate the "p" value by using unpaired *t*-test. The calculations were made by using Microsoft Office Excel 2007 and Graph Pad software. The complete analysis was done by extensively comparing the different parameters of MR severity.

RESULTS

This study included 114 patients at start, but due to death of 2 patients during follow up; 112 patients were available for data analysis. Both Group-A and B had 56 patients while both revascularization Subgroups-B1 and B2 had 28 patients.

Based on different parameters at baseline in Group-A; mild MR was present in 4 patients (7.14%) while moderate MR was present in 52 patients (92.86%). At the end of follow up; mild MR was present in 20 patients (35.71%) while moderate MR was present in 26 patients (46.23%). Severe MR developed in 10 patients (17.86%).

In Group-B at baseline; only 2 patients had mild MR and the rest 54 patients had moderate MR. At the end of follow up; mild and moderate MR were present in 36 (64.29%) and 16 patients (28.57%) respectively, while severe MR developed in rest 4 patients (7.14%).

When we compared the individual baseline parameters with follow-up parameters, none of the changes were statistically significant in Group-A patients (Table 1).

Group-B patients showed better results after 1 year of follow up and almost all of the parameters showed statistically significant reduction in severity (Table 2).

When we compared the overall result, MR grade improved in 60.71% of patients in revascularization group compared to 28.57% patients in medially managed group. 53.57% patients in Group-A remained in the same grade as before compared to 32.14% patients in Group B. The grade of MR deteriorated from moderate to severe in 17.86% patients in Group A, while only 7.14% of patients form group B deteriorated to severe grade. This outcome clearly favors revascularization over medical therapy. (Figure 1).

SUBGROUP ANALYSIS

Based on different parameters at baseline in Subgroup-B1; mild MR was present in 2 patients (7.14%) while moderate MR was present in 26 patients (92.86%). After 1 year of follow up, mild MR was present in 18 patients (64.29%) while moderate MR was present in 8 patients (28.57%). Severe MR developed in 2 (7.14%) patients.

In the Subgroup B-2; all 28 patients (100%) had moderate MR at baseline. At the end of follow up mild and moderate MR were present in 18 (64.29%) and 8 patients (28.57%) respectively, while severe MR developed in 2 patients (7.14%). Although these figures shows equal values after 1 year of follow up in both subgroups; we should remember the fact that in PCI subgroup there were 2 patients of mild MR from beginning; so overall improvement in MR grade occurred in 16 patients of PCI compared to 18 patients of CABG subgroup.

When we compared the Individual baseline parameters with follow up parameters; the results showed statistically significant improvement in both PCI and CABG subgroups (Table 3 & 4).

The overall subgroup analysis showed that revascularization by PCI is comparable to CABG in reducing the severity of MR grade. In Subgroup B1, the MR grade was improved in 57.14% of patients compared to 64.28% of patients in Subgroup B2. 35.71% patients from Subgroup B1

Table 1: MR severity parameters before and after one year of OMT

Parameter	At presentation		After 1 year		"*p*" value
	Mean	SD	Mean	SD	
MR Jet Area (% of LA)	28%	5.3	27%	9.7%	0.6341
VCW (mm)	3.98	0.96	3.94	1.74	0.9156
RgV (ml/beat)	40.61	7.92	39.18	13.71	0.6346
RgF (%)	35.43	5.04	34.61	9.83	0.6960
EROA (cm^2)	0.27	0.05	0.26	0.05	0.4575

LA: left atrium; VCW: vena contracta width; RgV: regurgitant volume; RgF: regurgitant fraction; EROA: effective regurgitant orifice area

Table 2: MR severity parameters before and after one year of Revascularization

Parameter	At presentation		After 1 year		"*p*" value
	Mean	SD	Mean	SD	
MR Jet Area (% of LA)	29%	5.1	23%	9.2%	0.0039*
VCW (mm)	4.24	0.88	3.41	1.45	0.0123*
RgV (ml/beat)	42.25	7.58	34.18	12.89	0.0061*
RgF (%)	37.14	4.85	30.07	9.36	0.0008*
EROA (cm^2)	0.28	0.05	0.23	0.08	0.0070*

LA: left atrium; VCW: vena contracta width; RgV: regurgitant volume; RgF: regurgitant fraction; EROA: effective regurgitant orifice area

Table 3: MR severity parameters before and after one year of PCI

Parameter	At presentation		After 1 year		"*p*" value
	Mean	SD	Mean	SD	
MR Jet Area (% of LA)	28%	5%	23%	9%	0.0130*
VCW (mm)	4.01	0.85	3.4	1.44	0.0588*
RgV (ml/beat)	40.29	7.32	34.21	12.93	0.0348*
RgF (%)	36	4.56	30.07	8.97	0.0029*
EROA (cm^2)	0.27	0.05	0.23	0.08	0.0290*

PCI: Percutaneous coronary intervention; LA: left atrium; VCW: vena contracta width; RgV: regurgitant volume; RgF: regurgitant fraction; EROA: effective regurgitant orifice area

Table 4: MR severity parameters before and after one year of CABG

Parameter	At presentation		After 1 year		"*p*" value
	Mean	SD	Mean	SD	
MR Jet Area (% of LA)	30%	6%	23%	10%	0.0025*
VCW (mm)	4.46	0.89	3.41	1.52	0.0026*
Reg Vol (ml/beat)	44.21	7.58	34.14	13.34	0.0010*
Reg Fraction (%)	38.29	5.03	30.07	10.09	0.0003*
EROA (cm^2)	0.30	0.05	0.23	0.09	0.0007*

PCI: Percutaneous coronary intervention; LA: left atrium; VCW: vena contracta width; RgV: regurgitant volume; RgF: regurgitant fraction; EROA: effective regurgitant orifice area

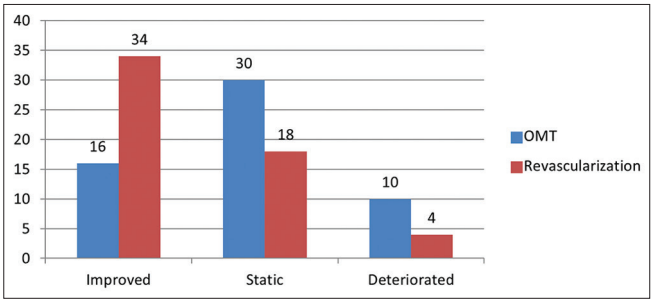

Figure 1: MR status after one year in medically managed and revascularized patients

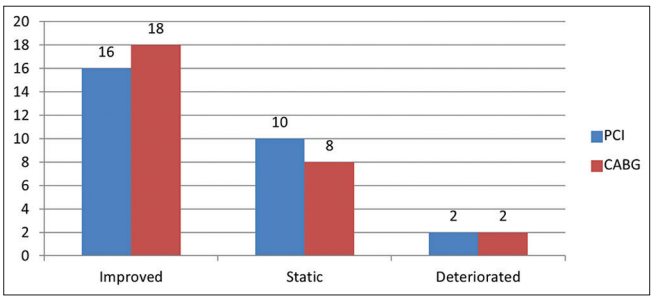

Figure 2: MR status after one year of follow up in PCI and CABG patients

and 28.57% patients from Subgroup B2 remained in the same grade as before. The grade of MR deteriorated from moderate to severe in 7.14% of patients from both subgroups. (Figure 2).

DISCUSSION

IMR is common with a reported frequency of 50% in the overall population; mild in 38% and moderate to severe in 12% of the patients.[2] After AMI, approximately 15% of mitral murmurs disappear by hospital discharge and another 15% are gone within several months.[27] The proper treatment of ischemic MR is often debated, and the relative utility of revascularization is uncertain.[5] Percutaneous or surgical revascularization has been associated with improved survival compared with medical therapy in patients with IMR[6,7] but the proper way of revascularization remains controversial.

The primary goal of our study was to evaluate the relation between various treatment strategies on progression of IMR. The findings of our study were compared and contrasted against several publications on similar issues. When we compared the degree of MR after one year in medically managed patients, improvement in MR grade occurred in only 28.57% of patients during follow up. As per analysis, this improvement was statistically not significant. At the same time when we compared the degree of MR in revascularized patients; improvement in MR grade was observed in 60.71% of patients which was statistically significant. This improvement was observed across all the parameters of MR severity. Also, MR grade deterioration was less in revascularized patients (7.14%) compared to medically managed patients (17.86%). This improvement in MR grade in revascularization arm at 60.71% was almost similar to the improvement observed in the study by Kang et al,[28] i.e. 67%. The subgroup analysis showed that there was almost similar improvement in both modes of revascularization across various MR severity parameters. Out of 28 patients in the PCI subgroup, there was improvement in 57.14% of patients while in CABG subgroup improvement was observed in 64.28%

of patients. Also, MR grade deterioration was similar in both subgroups (7.14%).

CONCLUSIONS

Revascularization; either in the form of PCI or CABG is better in improving grade of ischemic mitral regurgitation compared to medical management alone. Progression of ischemic MR also depends on its initial severity; none of the mild MR cases showed deterioration to moderate or severe category in our study. Also, PCI and CABG are almost equally effective in reducing the severity of MR across various echo parameters.

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JS- Concept and design of the study, critical revision of the manuscript; **SS-** Concept, collected data and review of literature, manuscript preparation and revision; **AR-** Literature review, statistical analysis and interpretation, manuscript revision; **MB-** Collected data, statistical analysis and review of the study.

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